- Breakeven sensitivity analysis was performed using the following assumptions:
  - There are no withdrawals in the venlafaxine XR group
  - There are no AEs in the venlafaxine XR group
  - There are no procedures in the venlafaxine XR group
- The model is considered robust if large changes in the parameter do not change the base case result

Results

Costs

The difference in treatment cost for escitalopram and venlafaxine XR are presented in Table 3.

Table 3. Cost Minimization Analysis

Total Costs	Escitalopram (n=127)	Venlafaxine XR (n=129)	Percent Difference
Cost daily dose (US $) (AWP)	2.24	3.05	-27%
Drug costs (Completed) (US $)	10,044	14,210	-29%
Drug costs (Withdrawn) (US $)	866	1,448	-40%
Cost of switching (1st Order) (US $)	4,284	6,300	-32%
Cost of procedures (SAE)	-	3,332	-100%
Total drug cost (US $)	10,910	15,658	-30%
AE costs (US $)	2,580	2,900	-11%
Total direct cost	17,774	28,190	-37%
Total direct cost/patient	140	218	-36%

SAE indicates serious adverse event; AE, adverse event.

Sensitivity Analysis

According to the breakeven point analysis, the cost minimization model is robust. Escitalopram remains the least costly treatment versus venlafaxine XR even if it is assumed that

- There are no withdrawals in the venlafaxine XR arm
  - Escitalopram savings=37%
- There are no procedures performed in the venlafaxine XR arm
  - Escitalopram savings=27%
- There are no AEs in the venlafaxine XR arm
  - Escitalopram savings=29%

Discussion

- Managed care total cost of treatment per patient is 36% less for patients treated with escitalopram compared with venlafaxine XR
- Savings were the result of lower drug acquisition costs, lower procedure costs, and fewer patient withdrawals
- Escitalopram had cost advantage in all resource use categories
- Treating 100 patients with escitalopram instead of venlafaxine XR would result in a cost savings of $7,800 which would allow for the treatment of an additional 56 patients at an average cost of $140 per patient

Conclusion

According to analyses of data using the cost minimization model based on a comparative study of escitalopram and venlafaxine XR, switching treatment for patients with GAD from venlafaxine XR to escitalopram may offer cost savings to managed care organizations. Cost savings were strongly influenced by drug acquisition costs, procedures, and study withdrawal. Further empirical research is needed to validate this model.

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A Comparison of Total Direct Medical Costs to Managed Care of Escitalopram Versus Venlafaxine XR Treatment in Generalized Anxiety Disorder

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Originally presented at the 25th Biennial Congress of Collegium Internationale Neuropharmacologicum July 9-13, 2006, Chicago, Illinois.

This poster was revised for accuracy and modified to reflect current pricing as cited in June 2006 *The Redbook. Pharmacy's Fundamental Reference.*

Abstract

Objective: To compare from a managed care perspective the the total direct medical costs of escitalopram (a selective serotonin reuptake inhibitor) and venlafaxine XR (a serotonin-norepinephrine reuptake inhibitor) as the first-line therapy for generalized anxiety disorder (GAD).

Methods: A total of 392 GAD patients (safety population) received at least 1 dose of double-blind flexible dose study medication: escitalopram (10-20 mg/day) or venlafaxine XR (75-225 mg/day) in a randomized prospective clinical trial. A cost minimization model that assumes no differences in study clinical outcomes was developed for the 2 treatment groups (escitalopram=127, venlafaxine XR=129) based on prospectively collected clinical data: drug use, adverse events (AEs), procedures and concomitant medications. Office visits required to treat adverse events and manage switching for patients who drop out were modeled. Treatment costs for AEs were taken from the literature. Procedure costs and office visits costs were derived from secondary databases. Costs for escitalopram and venlafaxine XR were assumed at average wholesale price (AWP), discounted 20% for managed care organizations, $2.24/day (20 mg) and $3.05/day (150 mg), respectively; the costs for concomitant medications were obtained from the Red Book (2006) and drugstore.com. To test the robustness of the model, 1-way sensitivity analysis was performed assuming a 50% reduction in the number of procedures and AEs.

Results: As assumed in the model no statistically significant clinical differences were observed in this trial. There were almost 2-fold more dropouts due to AEs with venlafaxine-XR than with escitalopram (13.2% and 7.1%, respectively; *P*=not significant). According to this cost minimization model, switching a patient from venlafaxine XR treatment to escitalopram decreases managed care total cost of treatment per patient by about 36%. One-way sensitivity analysis assuming that there were either no withdrawals, no procedures preformed, or no AEs in the venlafaxine XR treatment arm lends support to the analysis showing escitalopram treatment results in cost savings ranging from 29% to 37%, respectively.

Conclusion: Based on these analyses switching GAD patients treated with venlafaxine XR to escitalopram offers costs savings to managed care. Estimated costs savings per 100 patients switched to escitalopram from venlafaxine XR could result in a savings of $7,800. These cost savings could be used to treat 56 additional patients with escitalopram at an average total cost of $140 per patient.

Objective

Generalized anxiety disorder (GAD) is a highly prevalent and persistent disorder that is associated with considerable clinical disability and high economic costs.[1] A study was conducted to compare the selective serotonin reuptake inhibitor (SSRI) escitalopram and the serotonin-norepinephrine reuptake inhibitor (SNRI) venlafaxine XR as first-line therapy for GAD. A post hoc analysis of safety and resource utilization data was used to assess the total direct medical costs of treatment associated with escitalopram and venlafaxine XR from the perspective of a US managed care organization.

Methods

Clinical Background

A cost minimization model was developed based on a randomized, parallel-group, flexible-dose, multicenter trial. Patients with GAD as defined by *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV)[2] criteria were randomized to escitalopram or venlafaxine XR treamtent groups in a study that comprised a 1-week single-blind lead-in, an 8-week double-blind flexible-dose period, and a 2-week double-blind down-titration. The safety population consisted of 392 patients (age range, 18-65 years) with GAD (HAM-A score ≥20; HAM-A items 1 [anxious mood] and 2 [tension] score ≥2) who received at least 1 dose of double-blind flexible-dose study medication:

- Escitalopram 10-20 mg/day (n=127)
- Venlafaxine XR 75-225 mg/day (n=129)

Patient disposition and adverse event (AE) frequency were used in the cost analyses (Tables 1 and 2). There were approximately 2-fold more AE-related study withdrawals associated with venlafaxine XR than escitalopram; the difference was not statistically significant.

Table 1. Safety Population Patient Disposition

Disposition	Escitalopram (n=127)	Venlafaxine XR (n=129)
Completed, n (%)	102 (80.0)	96 (74.0)
Treatment duration, days	56	56
Withdrew due to any reason, n (%)	25 (20.0)	33 (26.0)
Treatment duration, days	19.7	16.6
Withdrew due to adverse event, n (%)	9 (7.0)	17 (13.2)

Table 2. Most Frequent Treatment-Emergent Adverse Events (Reported by ≥10% of Patients in Any Treatment Group)*

Preferred Term	Escitalopram (n=127) n (%)	Venlafaxine XR (n=129) n (%)
Patients with at least 1 TEAE	107 (84.3)	111 (86.0)
Ejaculation disorder (males only)†	11 (24.4)	15 (28.8)
Nausea	26 (20.5)	34 (26.4)
Headache	20 (15.7)	19 (14.7)
Insomnia	17 (13.4)	23 (17.8)
Impotence (males only)†	5 (11.1)	0 (0.0)
Somnolence	13 (10.2)	21 (16.3)
Mouth dry	11 (8.7)	24 (18.6)
Fatigue	8 (6.3)	14 (10.9)
Sweating increased	5 (3.9)	14 (10.9)

*Adverse events in safety population before down-titration.
†Escitalopram, n=45; venlafaxine XR, n=52.
TEAE indicates treatment-emergent adverse event.

Cost Minimization Model

A cost minimization model was developed based on the study results. The following assumptions were made:

- There is no clinical difference between the compared treatments
- Only costs need to be compared
- The treatment with the lowest cost is considered superior
- Costs are calculated from a the perspective of managed care organization

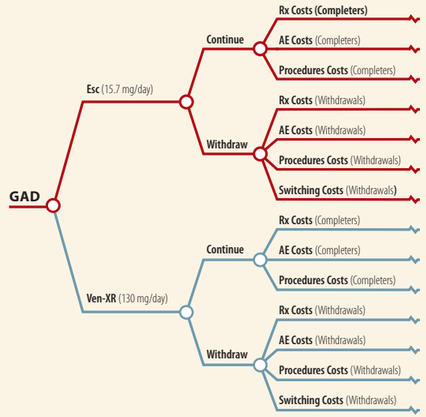
Treatment Options

Treated patients had the following options:

- Complete treatment
- Withdraw
  - Withdrawal due to AEs or to lack of efficacy.
  - All patients who withdrew were assumed to switch to another treatment.

The possible treatment pathways and their associated costs are presented in the figure.

Cost Minimization Treatment Pathway



Base Case Resource Use

A base case model was constructed based on data obtained from the trial and the model assumptions.

Four types of resource utilization data were considered for the model.

Treatment Drugs

- Drug utilization data was based on the observed mean daily dose used in the clinical trial (15.7 mg/day, escitalopram; 130 mg/day, venlafaxine XR)

Procedures

- Number and type of procedures observed in the trial regardless of cause

Treatment of AEs

- 25% of treatment emergent AEs were assumed to require a physician visit
- AEs that occurred in any treatment group are included in the economic analysis. Treatment options for these AEs were based on
  - Literature,[3] when available, or
  - Expert opinion
    - Medication to be used

Treatment Switch

- Patients who withdrew from the study, regardless of treatment arm, were assumed to switch to another drug, thus requiring additional office visits
  - Nonresponders = 2 office visits (1 visit to obtain prescription and 1 follow-up visit)
  - AE= 4 office visits (2 visits to treat the AE until AE is resolved, and 2 visits for the addition and management of the new drug)
- Office visit assumptions for switching were based on expert medical opinion
- New drug costs were not included

Base Case Costs

Cost per pill was assumed at average wholesale price (AWP), discounted 20% for managed care organizations[4]

- Escitalopram AWP=$2.81/day (20 mg); 80% AWP=$2.24/day
- Venlafaxine XR AWP=$3.83/day (150 mg); 80% AWP=$3.05/day
  - Mean daily dose was multiplied by drug costs and the number of drug treatment days for patients who completed or withdrew from the trial to obtain total drug costs

Procedure Costs

- Basal carcinoma procedure ($3,332)[5]

AE Treatment Cost

- Office visits assumed to be with a general practitioner at a cost of $63/visit[6]
- Costs of medication
  - AWP for concomitant medications[6]; used generic price when available
  - OTC costs from http://www.drugstore.com/[7]

Treatment Switch Costs

- Office visits assumed to be with general practitioner at the cost of $63/visit[6]

Sensitivity Analysis

- Sensitivity analysis was performed to test the robustness of the base case
- A breakeven point that delineated when a managed care organization would incur the same total cost for both treatments was calculated